

Malignant Pleural Mesothelioma: Current Perspectives and Future Prospects

Attapon Cheepsattayakorn^{1*} and Ruangrong Cheepsattayakorn²

¹10th Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand

²Department of Pathology, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand

*Corresponding Author: Attapon Cheepsattayakorn, 10th Zonal Tuberculosis and Chest Disease Center, Chiang Mai, Thailand.

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Malignant pleural mesothelioma (MPM), a rare aggressive tumor with increasing incidence is mainly associated with decades-long-term respirable asbestos exposure, approximately 40 years. The median survival ranges from 8 to 14 months. Only 12% of MPM patients with negative prognostic factors live longer than one year. Epithelioid tumors have a relatively favorable prognosis. The pathogenesis of MPM is multifactorial. Breathlessness is usually found in the early stage of the disease and is mainly due to a pleural effusion in around 70% of the patients at their presentations. Chest pain is also common and can be caused by pleural effusion or tumor. Current radiological imaging techniques are inadequate for screening and differential diagnosis of MPM and pleural plaques. Staging MPM is difficult due to limitations in current radiological imaging methods. The International Mesothelioma Interest Group staging classification and the tumor-nodes-metastases (TNM) classification of the Union for International Cancer Control (UICC) are the commonly classification systems used for MPM staging. Surgical thoracostomy (Video-assisted Thoracoscopic Surgery (VATS)), with additional mediastinoscopy is superior to the computed tomography (CT) in staging and diagnosis of MPM. VATS has sensitivity of 95% - 98% and specificity of 100% in the diagnosis of MPM, respectively. Cytological abnormalities are identified in both reactive and malignant lesions (MPM), and negative cytological examinations does not rule out MPM. Percutaneous needle pleural biopsy without radiological imaging guidance is only around 7% to 47%. A recent study suggested that liquid pleural biopsy could replace tissue biopsy in MPM diagnosis.

Measurements of circulating mesothelin, osteopontin, fibulin-3, high mobility group B1 (acetylated HMGB1), vascular endothelial growth factor (VEGF), reactive oxygen species, reactive nitrogen species, micro-ribonucleic acids (miRNAs)/cell-free circulating miRNAs (cfmiRNAs), tumor deoxyribonucleic acid (ctDNA), methylated deoxyribonucleic acid, tumor cells (CTCs) hold promise as potential biomarkers for the diagnosis and stratification of patients with MPM.

No curative treatment for MPM is currently unavailable. The systemic options include chemotherapy, targeted therapy, surgery, and radiotherapy. Surgery in MPM is much debated in its benefit and robust randomized trials data are urgently needed. Trimodality treatment for MPM consists of induction chemotherapy followed by extrapleural pneumonectomy (EPP) with subsequent hemithoracic radiotherapy. Nevertheless, a previous large randomized trials revealed that there was no difference in progressive-free survival or overall survival in MPM patients treated with neoadjuvant chemotherapy and EPP with or without radiotherapy. Targeted therapy to epidermal growth factor receptor antagonists and platelet-derived growth factor receptor inhibitors have demonstrated their efficacy. Mesothelin-targeted treatments are another interesting area in MPM that include anti-mesothelin immunotoxins (e.g. SSIP), chimeric antigen receptor T-cells targeted to mesothelin, mesothelin tumor vaccine (CRS-207), and mesothelin-specific monoclonal antibodies (e.g. amatuximab). Immunotherapy, such as pembrolizumab and tremelimumab have demonstrated impressively prolonged disease stability and disease control rates when used as first-, second-, or third-line treatment. Further exploration in combination of chemotherapy with immunotherapy, including exploring alternative immunotherapy agents and combinations in the treatment of MPM are urgently needed.

In conclusion, no reliable biomarker for the risk assessment and longitudinal monitoring of asbestos-exposed persons is available. Most of the mentioned biomarkers were studied in restricted patients' cohorts and the conclusive identification of robust circulating biomarkers for early diagnosis and prognostic stratification of the patients with MPM awaits validation in the large prospective studies. Several novel treatments are under investigation. It is likely that highly personalized treatment will involve the future treatment of MPM.

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